RADIATION RESEARCH **165**, 208–222 (2006)
0033-7587/06 $15.00

2004 Update of Dosimetry for the Utah Thyroid Cohort Study

Steven. L. Simon,[a,1] Lynn R. Anspaugh,[b] F. Owen Hoffman[c] Alan E. Scholl,[d] Mary B. Stone,[d] Brian A. Thomas[c] and Joseph L. Lyon[d]

[a] *Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, Bethesda, Maryland; and* [b] *Division of Radiobiology and* [d] *Department of Family and Preventive Medicine, University of Utah, Salt Lake City, Utah; and* [c] *SENES Oak Ridge, Inc., Oak Ridge, Tennessee*

Simon, S. L., Anspaugh, L. R., Hoffman, F. O., Scholl, A. E., Stone, M. B., Thomas, B. A. and Lyon, J. L. 2004 Update of Dosimetry for the Utah Thyroid Cohort Study. *Radiat. Res.* 165, 208–222 (2006).

In the 1980s, individual thyroid doses and uncertainties were estimated for members of a cohort of children identified in 1965 in Utah and Nevada who had potentially been exposed to fallout from the Nevada Test Site. That reconstruction represented the first comprehensive assessment of doses received by the cohort and was the first large effort to assess the uncertainty of dose on an individual person basis. The data on dose and thyroid disease prevalence during different periods were subsequently used in an analysis to determine risks of radiogenic thyroid disease. This cohort has received periodic medical follow-up to observe changes in disease frequency and to reassess the previously reported radiation-related risks, most recently after a Congressional mandate in 1998. In a recent effort to restore the databases and computer codes used to estimate doses in the 1980s, various deficiencies were found in the estimated doses due to improperly operating computer codes, corruption of secondary data files, and lack of quality control procedures. From 2001 through 2004, the dosimetry system was restored and corrected and all doses were recalculated. In addition, two parameter values were updated. While the mean of all doses has not changed significantly, many individual doses have changed by more than an order of magnitude.

INTRODUCTION

Nuclear weapons were tested above ground at the Nevada Test Site (NTS) from 1951–1958, and occasional large planned releases continued through 1968 as a result of the Plowshare cratering program. Concerns over potential health risks from radioactive fallout from the NTS resulted in Congressional hearings in 1957, 1959 and 1963 (*1–3*).

After the 1963 hearings, where possible injury to the thyroids of infants and children in Nevada and Utah was discussed, investigators from the U.S. Public Health Service (PHS) and the then Utah Division of Health ''. . . included a search for thyroid damage in their studies of the hazards to human health from exposure to fallout radiation'' (*4*). Weiss *et al.* (*5*) conducted a survey of surgically treated thyroid disease among residents of Utah ''. . . under the age of 30 at the time of thyroid surgery performed during the 15-year interval from January 1, 1948, through December 31, 1962.'' A comparison of rates of surgeries performed during 1948–1952 and 1958–1962 (persons operated on during the latter period were presumed to have been exposed) found substantial increases in the rates for the exposed persons for both thyroiditis (4.0 compared to 2.0 cases per 100,000) and thyroid cancer (2.3 compared to 0.6).

A cohort study (*4*) was implemented in the fall of 1965 with the initial goal of screening all children between the ages of 11 and 18 years attending junior or senior high schools in Washington County, Utah, which was judged to have been heavily exposed to fallout in 1953. Children were examined by a panel of three physicians; children suspected of having an abnormality were referred to a panel of three thyroid experts, and laboratory tests were also performed on children with suspected abnormalities and on selected groups of normal children. Follow-up examinations included surgery, if judged necessary. During the initial stages, mothers were interviewed to secure a detailed residence history, but no attempts were made to define dietary history. The cohort study by Weiss *et al.* is now referred to as Phase I of the Utah Thyroid Cohort Study (TCS).

Phase II of the Utah TCS began after the report of an excess in leukemia deaths among exposed children in southwestern Utah (*6*); this resulted in the U.S. National Cancer Institute (NCI) funding the University of Utah to conduct a case-control study of leukemia in Utah and to recreate the Utah TCS for those examined in Phase I. Of the original students examined during Phase I, 4180 were located during the 1980s. Of those, 3122 were re-examined to form Phase II of the Utah TCS. Part of the goal of Phase II was to examine the disease data for a dose response; hence each subject had to be assigned an estimate of thy-

[1] Address for correspondence: National Cancer Institute, 6120 Executive Blvd., Room 7100 Executive Plaza South, Bethesda, MD 20892–7230; e-mail: ssimon@mail.nih.gov.

roid dose received from NTS fallout. To enable dose estimates to be made, a detailed milk consumption history of the subject (or his mother during pregnancy) was obtained from a parent or other respondent for each subject covering the period from conception to age 18 years. A survey of milk producers in southwestern Utah was also conducted by the University of Utah (*7*) to provide input data for a detailed dose assessment model (*8*). The findings from the Phase II dosimetry were published by Till *et al.* (*9*) and the findings from the epidemiological analysis were published by Kerber *et al.* (*10*). The dose estimates used by Kerber *et al.* are now known to be faulty (see below), and the major topic of this paper is the correction of those doses. This phase of the study is designated as Phase IIR (revised).

In 1997, the NCI (*11*) reported that radioiodine contamination from the NTS had likely contaminated the milk supply in all 48 contiguous states to different degrees and that doses comparable to those received by children living in Washington County in 1953 had likely been received in states north and east of Nevada as well as Utah. That report became the subject of a U.S. Senate hearing (*12*) and resulted in a charge (*13*) to the Centers for Disease Control and Prevention (CDC) to ''. . . continue the follow-up study of the Utah cohort exposed to fallout from the Nevada Nuclear Weapons Test Site.'' As a result, the CDC funded the University of Utah under a Congressional mandate in 1998. That activity, now designated as Phase III, is presently under way. Phase III findings will be reported in the future, when examinations and other dosimetry activities are completed.

The 1998 mandate implied that the databases and dosimetry programs used in the Phase II study in the mid-1980s should be restored and made operable. However, the dose estimates of the Phase II study, having been calculated in the mid-1980s using software and computer hardware no longer available today, could not be recalculated without using new software and new computers. When Phase II doses were recalculated in 2001, it was realized that parts of the computer programs used in the 1980s had not functioned properly and that some of the secondary data files used in the prior calculations had been corrupted; this resulted in reported dose estimates (*9*) containing numerous errors. Hence the dose estimates used by Kerber *et al.* (*10*) in the epidemiological analyses of Phase II also suffered from the same deficiencies.

New understanding of some model parameters and pathways suggested the need to update the Phase II dose models for the Utah TCS at the same time that the Phase II algorithms were being reprogrammed. The task of updating the models and software was carried out between 2001 and 2004 and resulted in what is designated here as Phase IIR dosimetry. The Phase IIR dosimetry includes a number of minor modifications to the earlier dose models but, more importantly, incorporates a detailed quality assurance/quality control (QA/QC) program to ensure proper operation. Though some corrections and improvements to the original Phase II methodology were made, the primary intent of this work was to implement correctly the originally intended methodology of Phase II. The purpose of this paper is to document the recent changes made to the Phase II dosimetry system and the results of recalculating all doses.

The Phase IIR dose estimates have been used to re-evaluate the epidemiological findings reported in ref. (*10*) and are being prepared for publication.

METHODS

The methodology for the Phase II dosimetry calculations was described in detail by Simon *et al.* (*8*) and summarized by Stevens *et al.* (*14*). Those details will not be repeated here, but information on the foundation of these techniques is provided here as well as a description of the revisions to those methods that have been implemented recently.

The protection of human subjects during Phases II and III of this overall project has been reviewed, approved and monitored by the University of Utah Institutional Review Board (IRB). During 2 years of this study, when it had been funded as a cooperative agreement with the CDC, approval was also received from the CDC IRB. All questionnaires developed for this study have been approved by the U.S. Office of Management and Budget.

Technical Basis of the Phase II Dosimetry

The methodology for the dose assessment in the Phase II TCS built on the results of the work of others since there had been many previous investigations of the dose to the thyroid from fallout from nuclear weapons tests and other releases of radioiodines. The foundation of the dose reconstruction method for exposures from fallout had been developed by Knapp (*16*) in his pioneering effort to reconstruct thyroid doses to infants in Utah and Nevada after tests in 1962. The important concept developed by Knapp was that there was a systematic relationship between the amount of ^{131}I in milk or human thyroids and the normalized measured external γ-ray exposure rate within the fallout field (normalized refers to adjustment of measurements made at different times to a common time, usually 12 h after the detonation). Prior to Knapp's work, it was known that ^{131}I might be causing significant exposures, but there had not been success in measuring the concentration of ^{131}I in milk. While the doses from ^{131}I from the tests in 1962 were significant, the major concern came from application of the method to the tests that had been conducted in 1951, 1952, 1953, 1955 and 1957.

The next major advance in the development of the methodology for dose reconstruction from fallout from nuclear tests followed when the Department of Energy established the Off-Site Radiation Exposure Review Project (ORERP) in 1979 to collect all relevant information and to perform a comprehensive reconstruction of doses to representative persons in the near downwind area of the Nevada Test Site (NTS) (*16*). The conduct of the ORERP included open to the public Federal Advisory Committee meetings that resulted in numerous publications (*17–27*) that established much of the methodology used in the Utah Phase II study as well as crucial databases of input data (*28–30*).

Calculations of dose from external γ-ray exposure for representative persons had been performed comprehensively while the tests were ongoing [see refs. (*31, 32*)], so not a great deal of new methodology was required. The primary technical problem the ORERP faced was how to estimate dose from the ingestion of radionuclides in food products. Because measurements of the concentration of radionuclides in food were not available, an indirect approach was developed.

The solution to estimating intake of radionuclides from fallout was found in the concepts developed by Knapp (*15*) that specified that there was a correlation between the amount of ^{131}I in milk and the external γ-ray exposure rate normalized to 12 h after the explosion (typically 12 h after detonation, or H+12). That concept was broadened to estimate con-

centrations of all radionuclides but was narrowed to the estimation of the amount of a radionuclide per unit area on the ground at a specified time. If the amount of a radionuclide on the ground (including vegetation) is known, then the passage through food to humans can be calculated with due allowance for ecological and agricultural conditions. Thus the concept of the ORERP reconstruction of dose from ingestion was the following simple equation:

$$D_{ijk} = \dot{X}_{12} \times ND_j \times I_{jk} \times DCF_{ijk}, \quad (1)$$

where D_{ijk} is the absorbed dose (Gy) to organ i of a person of age k from radionuclide j; $\dot{X}_{12}$ is the measured external γ-ray exposure rate (C kg^{-1} s^{-1})[2] normalized to H+12 h; ND_j is the normalized deposition of radionuclide j normalized to unit exposure rate at H+12 h (Bq m^{-2} per C kg^{-1} s^{-1}); I_{jk} is the integrated intake by ingestion of radionuclide j by a person of age k per unit deposition of radionuclide j (Bq per Bq m^{-2}); and DCF_{ijk} is the dose conversion factor for the dose to organ i from ingestion of radionuclide j by a person of age k (Gy Bq^{-1}).

The estimation procedure for internal dose required data on the external γ-ray exposure-rate measurement as input, since this was the only measurement that had been made consistently since the very first event at the NTS. Although the method can be used to estimate doses from all fission and activation-product radionuclides, the method was applied in the TCS Phase II study only for ^{131}I and ^{133}I.

The ORERP was also successful in collecting and translating the historical exposure-measurement data into an electronic database (*34, 35*). That laborious task included converting handwritten notes, and its completion was crucial to the overall ORERP project. Another activity was to examine the original exposure-rate data for the more important tests and to reconstruct fallout patterns. This comprehensive examination of the data led to several major improvements [see ref. (*25*)]. Because not every location of interest had an actual measurement of external γ-ray exposure rate, the survey-meter readings and the fallout patterns were used to infer ''readings'' at other locations by a variety of methods, including kriging. This work led to the creation of the ''Town Data Base'' (TDB) (*28, 30*), which included a ''reading'' for every location, even ranches, within populated areas within Washington County, Utah, and the Nevada counties of Clark, Lincoln, Nye and Esmeralda. Data for many other locations are also within the TDB, but another method was subsequently found to reconstruct doses at locations beyond those five counties.

Based on the assessment of unclassified and classified information (*36*) on the designs of each nuclear device, radiochemical studies of nuclear debris, and samples of radioactivity collected by aircraft during cloud penetration, Hicks (*18, 23, 37*) developed a catalog for every atmospheric event at the NTS. The catalog was a set of tables that gave values of ND_j for up to 177 radionuclides for 31 periods ranging from time of detonation until 50 years afterward. The mix of radionuclides was tracked through time by a modified version of the ORIGEN Code (*38*). The normalization to external γ-ray exposure rate was accomplished with the use of Beck's (*17*) calculations of exposure rate per unit deposition for each of the 177 radionuclides that have significant emission of γ radiation. The tables prepared by Hicks have been widely used for virtually all dose reconstructions relating to the NTS.

Later, the ORERP study was extended to areas beyond those adjacent to the NTS. That effort was also of great value to the Phase II TCS and was made possible by the development of the means to separate the NTS portion of the ^{137}Cs deposition density (Bq m^{-2}) due to regional fallout. The means of using contemporary measurements of ^{137}Cs were greatly enhanced by work performed by Krey and Beck (*39*), in which it was found that plutonium deposited as part of NTS fallout had differing ratios of ^{240}Pu to ^{239}Pu compared to global fallout. Hence it became possible to separate global from regional fallout and to estimate the fraction of total ^{137}Cs that had come from the NTS. This advance and demonstration led to the undertaking of the ORERP Phase II activities, and the study domain was expanded to the entire states of Nevada, Utah, Arizona, New Mexico and parts of Colorado, Wyoming, Idaho, Oregon and California.

Much additional work was done to examine other sources of additional data, including the data from the gummed-film network (*19*), and meteorological models were used cautiously to extend the existing fallout patterns (*40*). These and many other sources of data and information were used to derive the County Data Base (CDB) (*29*), which within the study domain lists the estimated external γ-ray exposure rate and the time of arrival at each county for each event. Because of uneven deposition in counties close to the NTS, several counties were split into two or more subsections.

To be as independent as possible, the Utah TCS did not adopt the ORERP methods completely but rather undertook an independent development effort that included the foundations laid by the ORERP with modification useful for deriving individual doses for subjects of the TCS [see ref. (*8*)]. Nevertheless, given the input data available, the TCS Phase II study relied heavily on ORERP data [for example, refs. (*23, 24*)], and particularly on the TDB (*28, 30*) and the CDB (*29*). Because the Phase II TCS needed similar data for other locations, the Other Locations Data Base (OLDB) [see ref. (*8*)] was developed to fill out data for the remaining states of Colorado, Wyoming and Idaho. Thus the Phase II study relied on the ORERP data for most values of $\dot{X}_{12}$ and all values of ND_j. The Utah TCS developed independent methods of estimating I_{jk} and DCF_{ijk}.

Specifics of the Phase II Dosimetry Model

The dosimetry model for the Phase II TCS, while based largely on prior work, was developed specifically for the epidemiological study. The goal of the dosimetry was to calculate the total NTS-related thyroid absorbed dose (Gy) from fallout deposited at the locations where each member of the cohort derived their milk and vegetables and at their residence for calculation of inhalation dose and external exposure. The Utah TCS was the first epidemiological study of environmental radiation exposure that characterized the uncertainty of the total estimated dose on an individual basis (*14*).

Several specific aspects of Phase II of the TCS, including some new developments, are worth noting here. The TCS was the first epidemiological investigation to use the methods of Hicks and the ORERP for estimating deposition density. To facilitate that for the many sites of milk production, the Hicks data for all NTS tests were fitted to time-dependent functions so that the ND_j values could be predicted reliably for all times of fallout deposition (*8*). The interception of fallout by vegetation consumed by dairy animals was modeled using historical data, and a function was derived to predict an increasing level of interception at greater distances and/or longer fallout travel times (*41*). Though that analysis probably represented the most significant difference from the methods used by the ORERP, the interception data were brought to the attention of the Utah Phase II investigators by ORERP investigators. That was but one example of useful cross-fertilization from the DOE-funded studies that were ongoing at that time. The time-integrated concentrations (I_{jk}) of ^{131}I and ^{133}I were estimated by analytic solutions (*8*) to differential equations using specific input data from a survey of over 300 milk producers in the study region (*7*). The uncertainty of each total dose was derived on an individual basis from a method combining Monte Carlo simulations (for environment transport) and analytic error propagation (for dose) (*14*).

Another marked difference in the ORERP and the Utah Phase II methods was in the treatment of dose from inhalation. After extended study of the problem, ORERP investigators concluded that there was no reliable correlation between air concentration and deposition and only calculated example results where the air concentrations of radioactivity had been measured either by cascade impactors or by high-volume air samplers. Because the dose from inhalation to a hypothetical milk-drinking individual was a small fraction of dose due to ingestion, no comprehensive effort was made in the ORERP to calculate doses from inhalation. The object of the Utah TCS, however, was to assess completely the doses for

[2] The units of C kg^{-1} s^{-1} are coulomb per kilogram per second, which is the SI Unit for exposure rate; 1 C kg^{-1} s^{-1} is equal to 1.40×10^{10} mR h^{-1} (*34*). The original measurements were always reported in units of mR h^{-1}.

the subjects enrolled in the study. Some persons in the Utah study did not drink milk; thus it was considered more important to have an estimate of dose by inhalation, even if that estimated dose was very uncertain. The model developed (*8*) relied on the concept that the particle-size distribution was dominated by increasingly smaller and thus more respirable-sized particles with increasing distance (or travel time). Thus the absorbed dose by inhalation per unit of deposition density was modeled to increase with distance or travel time from the NTS detonation sites.

Estimations of Thyroid Dose by Location and Phase of Study

In the Phase II TCS, which was conducted in the mid-1980s, the dosimetry system was designed to estimate total NTS-related doses for 3545 subjects who resided at some time during the study period (January 1, 1951, through December 31, 1962) in Utah, Arizona, Nevada, Idaho, New Mexico, Wyoming and Colorado. At all other locations, doses from NTS fallout were assigned as zero.

In the Phase II epidemiological analysis, only 2473 of the 3545 subjects were included (*10*). For an individual to be included in the analysis, it was required that the following criteria be satisfied: (1) the subject was Caucasian, (2) the subject had a thyroid examination in Utah, Arizona or Nevada, and (3) the subject had no radiation treatment prior to the thyroid examination.

In the Phase II analysis, 66 of the 2473 subjects had been assigned zero doses because they lived outside the seven-state area. Conversely, the Phase IIR analysis group includes 2497 subjects—2470 of the Phase II group (three of the 2473 were excluded, because they lived outside the contiguous U.S. during the study period) and 27 additional subjects whose race and/or disease information had previously been coded incorrectly.

Phase IIR Modifications

In the work described here, a few modifications have been made to the Phase II dosimetry methods (*8*) to (1) correct programming errors and corrupted secondary data files and (2) to update the earlier dose estimates with recent information while still retaining the fundamental design of the Phase II dosimetry algorithm. The updated calculations, referred here as Phase IIR, include changes in eight specific areas, the first two being corrections, the next six being updates: (1) correction of Phase II programming failures and corrupted data files, (2) correction of the analytic equation describing the time-integrated concentration of radioiodine in milk after ingestion of soil by dairy animals, (3) update of one of three deposition databases, (4) use of the National Cancer Institute's dose calculator (*42*) to provide estimates of thyroid dose for subjects for periods of their exposure history during which they lived outside of the original domain of Phase II, (5) modification of the method to estimate each subject's average consumption rate of fresh leafy vegetables, (6) modification of the factor describing the transfer of radioiodine to human breast milk, (7) modification of the methodology used to address correlations among exposure pathways and shots for the purpose of calculating the variance on individual doses, and (8) modifications on how the uncertainty of subject move dates is propagated. Each of the eight topics of modification is described briefly. In addition, the development and implementation of a comprehensive QA/QC program is discussed.

1. Correction of Phase II programming failures and corrupted data files

The Phase II computer programs used to estimate the final doses (*9*) in the mid-1980s were found in 2001 to have inadvertently not calculated the dose from cows' or goats' consumption of pasture grass. We believe, however, that the algorithm used in Phase II to calculate the time-integrated concentration of ^{131}I in milk from soil ingestion overestimated the true contribution of that pathway (see section below). Hence the overestimate of ^{131}I by soil compensated in part for the improper program operation that omitted the contribution from pasture grass. Both the pasture grass and soil ingestion algorithms and programs were modified to ensure proper operation in the Phase IIR calculations reported here.

In addition, many of the secondary data files used in calculations performed in the 1980s were found to have been corrupted. Most of the corrupted files were associated with information used to calculate deposition of radioiodines. The corrupted files were rederived from original sources.

2. Ingestion of soil by dairy animals

During the restoration of the Phase II dosimetry system, the analytic expression for estimating the time-integrated concentration of radioiodine in dairy animals' milk after inadvertent ingestion of soil was found to be incorrect. A correct expression was subsequently derived as the solution of a first-order differential equation describing the time rate of change of activity in soil that received initial deposition not intercepted by vegetation, and a continuing contribution from fallout that is weathered from the surfaces of plants. The corrected expression for the time-integrated concentration in milk from ingestion of radioiodine in soil is

$$C^*_{ms} = GD \times k_s \left[\frac{e^{-\alpha Y_P}}{\lambda} + (1 - e^{-\alpha Y_P}) \left(\frac{1}{\lambda} + \frac{1}{\lambda + \lambda_w} \right) \right] f_m \times \dot{I}_s, \quad (2)$$

where C^*_{ms} is the time integrated concentration of isotope-specific radioiodine in milk (Bq day liter^{-1}); GD is the isotope specific ground deposition (Bq m^{-2}); k_s is the proportionality constant (m^2 kg^{-1}); α is the vegetation-interception constant (m^2 kg^{-1}); Y_P is the vegetation yield (dry) (kg m^{-2}); λ is the isotope-specific radiological decay constant (day^{-1}); λ_w is the weathering decay constant (day^{-1}); f_m is the feed-to-milk transfer factor (day liter^{-1}); and $\dot{I}_s$ is the rate of soil ingestion (kg day^{-1}) by milk-producing, grazing animals.

Use of the previously used incorrect equation resulted in an overestimate of the amount of soil-derived radioiodine in milk. The magnitude of the overestimate depended on the time of arrival of fallout at a particular location, upon which the value of α in Eq. (2) depends. At the maximum value of α of 3.0 m^2 kg^{-1}, the effect of the error was to overestimate the amount of soil-derived ^{131}I in milk by a factor of 2.3.

The assumption was made for the Phase II algorithms that all soil ingested by dairy animals was from the top 1 mm of the soil surface. That assumption was based on the documentation for the PATHWAY computer code (*20*), and the same assumption had been used by the NCI (*11*) for reconstruction of doses from dry deposits of radioactive fallout across the contiguous U.S.

We re-evaluated the Phase II assumption that dairy animals consume soil from a depth of 1 mm and concluded that a revision to that assumption was necessary. A depth of 1 mm might be appropriate for soil ingested during grazing of pasture vegetation, where soil particles have been resuspended by wind and rain and deposited on the surfaces of vegetation. However, soil is also ingested by dairy animals when root material is consumed during grazing and from direct consumption of soil while trampling and wallowing. In such situations, grazing animals can ingest soil from depths considerably deeper than the first 1 mm of the soil surface. In general, modification of the assumption on depth serves to dilute the calculated amount of radioiodine ingested per unit of soil consumed.

In the absence of literature citing direct observations on the depth from which soil is routinely ingested by cows and goats, we have concluded that the Phase II assumption of 1 mm is an extreme value that is likely to lead to a substantial overestimation of the ingestion of ^{131}I from soil. For the purposes of Phase IIR, a more realistic effective depth of soil intake is assumed to be 3 mm (geometric mean), with an uncertainty assigned equal to a geometric standard deviation (GSD) of 1.6 to allow for the possibility that the true depth may be as shallow as 1.2 mm or as deep as 8 mm (95% credibility interval).

Assuming an effective depth of 3 mm from which soil is ingested produces a value for k_s of 0.26 m^2 kg^{-1} given a density of surface soil of 1.3 g cm^{-3}. Thus the credibility interval for k_s is 0.1 to 0.7 m^2 kg^{-1}. This revised value resulted in estimates of the concentration of radioio-

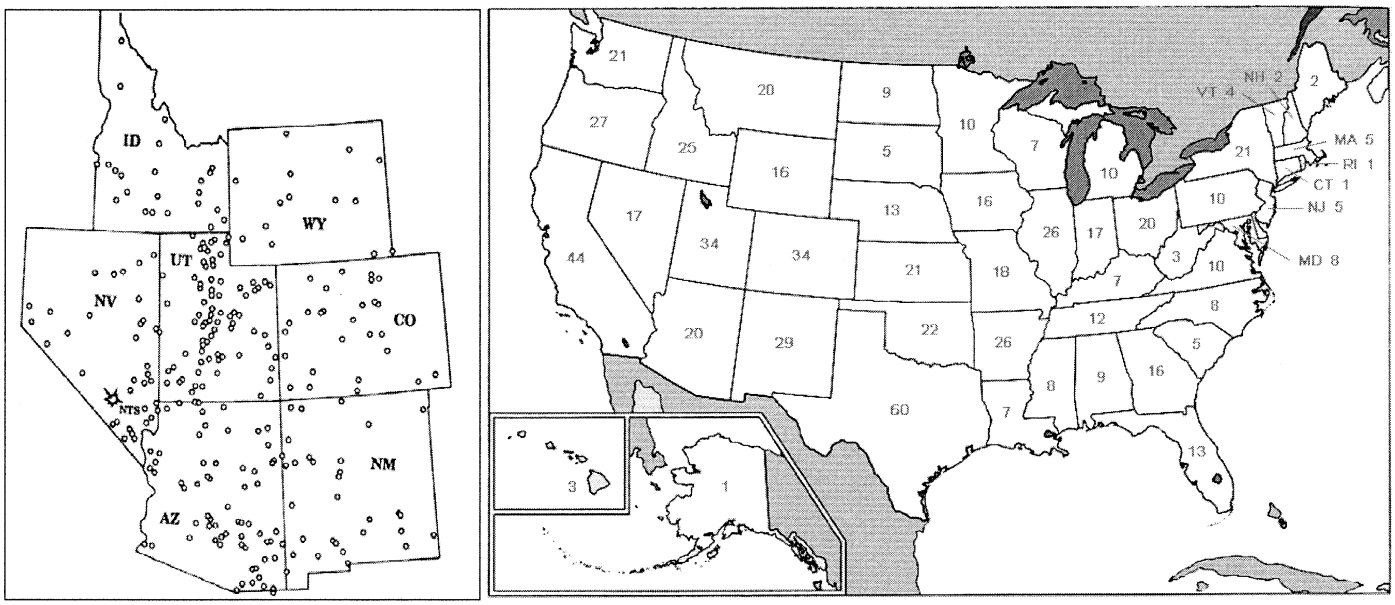

FIG. 1. Towns and states where study subjects resided during the study period (January 1, 1951, through December 31, 1962). Locations where any subject resided in the seven-state area are shown as small circles in the left panel, and other states of residence in the right panel. Numbers in states represent the number of counties in that state where one or more study subjects lived for at least 1 month during the study period. The number of counties shown is larger than the actual number of counties in some states due to our subdivision of counties where necessary to account for uneven deposition.

dine ingested by grazing animals that were substantially less than those estimated in Phase II, for which the nominal value of k_s had been assumed to be 1.0 m^2 kg^{-1}.

3. Update of deposition database

In the Phase II dosimetry system, three databases of deposition information were used depending on location. One database, termed the Other Locations Database (OLDB), was to provide estimates of external γ-ray exposure rate at H+12 h in the areas of Colorado, Wyoming and Idaho not covered by the County Database (CDB). The derivation of the OLDB in the 1980s for the Phase II study had used ^{137}Cs deposition density derived from gummed-film data from Beck (*19*). Later, Beck[3] made numerous corrections to the data published previously (*19*) and also made data available for additional locations throughout the U.S. The data we used for the re-derivation of the OLDB were from stations in Washington, Montana, Colorado, Nebraska and South Dakota that had not been considered during Phase II of the TCS. Our rederivations of ^{137}Cs depositions were generally based on two nearby locations where gummed-film measurements had been made; data on ^{137}Cs deposition at the gummed-film stations were weighted by the reciprocal of the distance from the site of interest to the site of the gummed-film station. Estimates of fallout time of arrival (*TOA*, h) were also based on the gummed-film data for nearby stations or on fallout trajectories published in ref. (*19*). To be consistent with the TDB and the CDB, estimates of ^{137}Cs deposition were converted to external γ-ray exposure rate at H+12 h by dividing by the ratio of ^{137}Cs deposition to external γ-ray exposure rate at H+12 h as given by Hicks (*37*). The changes described here resulted in a completely rederived version of the OLDB for the Phase IIR dosimetry calculations.

4. Use of the National Cancer Institute's NTS dose calculator

In the Phase II TCS, doses from NTS fallout were assigned as zero when subjects resided outside of the area for which deposition data were available in the three deposition databases (TDB, CDB and OLDB). Though study subjects did live in many locations (primarily towns) within the seven-state primary area (Fig. 1, left panel), the number of residence locations across the U.S. (Fig. 1, right panel) had largely been unappreciated. Moreover, it was previously believed that doses received outside of the seven-state areas (and small parts of California and Oregon) would be small compared to doses received within these areas. The premise of that assumption was unverified for many years, however, due to the lack of deposition data in other states that could be used to estimate doses for comparison purposes. Examination of the complete set of residence locations during the study period (Jan. 1, 1951, through Dec. 31, 1962) reveals that study subjects lived in all states of the U.S. (including Hawaii and Alaska) except for Delaware (Fig. 1, right panel).

Nationwide deposition data obtained from archival data sets were later analyzed and used by the NCI as the basis for their publication (*11*) on doses received by U.S. residents from NTS fallout. The same data were used as the basis for developing a web-based thyroid dose and thyroid cancer risk calculator (*42*). The Phase IIR study has used the NCI calculator as a tool to improve the data set on total cohort doses by incorporating dose estimates for those intervals of time when study subjects lived outside of the immediate study area.

5. Consumption rate of fresh vegetables

Individual information on the consumption rate of fresh vegetables of cohort members during the exposure period was not available from subject interviews. The person-specific data that concern the consumption of fresh vegetables that are available from interviews were whether leafy vegetables were eaten from locally produced sources during each residence; months of the year those vegetables were eaten; percentage of fresh leafy vegetables consumed that were from a local garden; and number of days per week that locally produced vegetables were eaten.

This available information on cohort members was used to adjust daily annual-averaged and age-dependent consumption rates for leafy vegetables summarized from market-basket surveys [taken from Rupp (*43*)] to obtain an estimate of personal consumption for the time of exposure to fallout from a given shot. The adjustments were made using a product of ratios:

[3] H. L. Beck, New York City (retired, U.S. Department of Energy's Environmental Measurements Laboratory), personal communication, 2001.

$$\dot{I}_{vs} = \frac{F_{vc(d)}}{F_{vc(d)}} \times \frac{N_{mo}}{F_{vc(m)}} \times \frac{\bar{\dot{I}}_{v(\text{cohort})}}{\bar{\dot{I}}_{v(\text{USA})}} \times \bar{\dot{I}}_{v(\text{USA})} \times k_{\text{dry/wet}}, \quad (3)$$

where $\dot{I}_{vs}$ is the subject-specific consumption rate of fresh leafy vegetables [kg (dry weight) day^{-1}]; $F_{vc(d)}$ is the frequency (days per week) that a subject consumed fresh leafy vegetables during the months when fresh leafy vegetables were available locally; $\bar{F}_{vc(d)}$ is the average frequency (days per week) that subjects in the cohort consumed fresh leafy vegetables during the months when fresh leafy vegetables were available locally; N_{mo} is the number of months in a year (i.e., 12); $F_{vc(m)}$ is the number of months per year when local fresh leafy vegetables were available; $\bar{\dot{I}}_{v(cohort)}$ is the annual average daily consumption rate [kg (dry weight) day^{-1}] of locally produced leafy vegetables for the cohort; $\bar{\dot{I}}_{v(USA)}$ is the annual average daily consumption rate [kg (dry weight) day^{-1}] of locally produced leafy vegetables for the U.S. from Rupp (*44*); and $k_{dry/wet}$ is the average dry weight to fresh weight (0.057 kg_{dry} kg_{wet}^{-1}).

In Stevens *et al.* (*14*), the values reported by Rupp (*43*) had been assumed to be on a dry weight basis and used without adjustment for differences between the consumption rate of the subject and that reported as an annual averaged daily rate. The adjustment for the difference between dry and wet weight consumption rate using $k_{dry/wet}$ for Phase IIR dose calculations results in person-specific exposures that are substantially lower than those estimated in Phase II. The other adjustment ratios generally result in modifying the daily intake rates averaged over a year to daily intake rates averaged for the period when leafy vegetables from local sources are consumed.

6. Breast milk transfer factor

The Phase II dosimetry system used the method described by Ng *et al.* (*44*) to estimate a coefficient to describe the transfer of radioiodine into the milk of lactating women. The method integrates a function (from zero to infinity) that describes the loss rate of the radioiodine in mother's milk from an acute dose expressed as a fraction of the total intake secreted per liter. With use of limited data from three publications, the Phase II estimate of f_m for ^{131}I was 0.02 day liter^{-1} while the value for ^{133}I, adjusted for its shorter half-life, was 0.0094 day liter^{-1}. Since the publication of the Phase II methods (*8*), additional information on the transfer of radioiodine to human breast milk has been collected and analyzed by Simon *et al.* (*45*). The value of 0.37 day liter^{-1} (GSD = 1.5) for f_m of ^{131}I into human breast milk as recommended by Simon *et al.* is used in the Phase IIR calculations presented here. The value we have assumed for ^{133}I is 0.17 day liter^{-1} (GSD = 1.5).

7. Correlations

In the Phase II dosimetry system, uncertainty was propagated by a combination of Monte Carlo and analytic error-propagation techniques, and the overall distribution of uncertainty for each individual was assumed to be lognormal. The end result of the dosimetry calculations was an estimate of the mean absorbed dose (arithmetic and geometric means were preserved) for each subject and the standard deviation (both arithmetic and geometric standard deviations were calculated) to describe the uncertainty of each estimated dose.

To estimate the total dose for individual subjects, mean estimates of each person's uncertain doses for different pathways were summed while the total uncertainty in dose was estimated by summing the individual pathway variances including the covariance terms. Covariance terms explicitly included correlations among pathways, though values for correlations were chosen based on professional judgment.[4] The equations used for Phase IIR to estimate total dose from the pathways considered and the variance in total dose are given in Eqs. (4) and (5). Table 1 gives the correlation values assumed for the Phase IIR calculations.

TABLE 1
Matrix of Correlation Coefficients used for Summing Variances across Pathways

Pathway	Milk	Vegetables	Inhalation	External
Milk	1			
Vegetables	0.3 or 0.8[a]	1		
Inhalation	0.3	0.3	1	
External	0.3	0.3	0.3	1

[a] When milk is obtained locally.

$$D_{t1} = D_{m1} + D_{v1} + D_{i1} + D_{e1} \quad \text{by event}, \quad (4)$$

where D_{t1} is the arithmetic mean dose to thyroid of subject by event; D_{m1} is the arithmetic mean dose to thyroid of subject from milk consumption by event; D_{v1} is the arithmetic mean dose to thyroid of subject from vegetable consumption by event; D_{i1} is the arithmetic mean dose to thyroid of subject from inhalation by event; and D_{e1} is the arithmetic mean dose to thyroid of subject from external radiation by event.

$$S_{t1}^2 = S_{m1}^2 + S_{v1}^2 + S_{i1}^2 + S_{e1}^2 + 2r_{m1,v1}S_{m1}S_{v1} + 2r_{m1,i1}S_{m1}S_{i1} + 2r_{m1,e1}S_{m1}S_{e1} + 2r_{v1,i1}S_{v1}S_{i1} + 2r_{v1,e1}S_{v1}S_{e1} + 2r_{i1,e1}S_{i1}S_{e1} \quad \text{by event}, \quad (5)$$

where S^2 is the variance of dose to thyroid of subject by pathway and by event (indices as above) and r is the correlation coefficient among pathways by event (indices as above).

In the Phase II dosimetry, doses received by an individual over time from different nuclear tests were assumed to be correlated,[5] primarily as a means to account for consistency or similarity of individual thyroid uptake and mass throughout the years of exposure. In the Phase IIR calculations, a modification was introduced for an assumed numerical value of a temporal correlation coefficient. (Note: In this context, temporal correlation, also known as serial correlation or autocorrelation, describes the correlation among values of dose to a single individual over time.) The temporal correlation coefficient for Phase IIR is estimated according to the following relationship:

$$r = 0.3 + 0.55e^{-1.83t}, \quad (6)$$

where t is the elapsed time in (years) between successive shots.

The maximum temporal correlation would be 0.85, for tests occurring within a few days of one another. The correlation would be reduced to 0.52 after 6 months and to 0.39 after 1 year. This correlation function is applied to all tests to which a person was exposed at a single location.

8. Uncertainty of subject-related dates

In our effort to implement the Phase II dose reconstruction algorithm used to produce the results in Kerber *et al.* (*10*), we found that the calculation of dose and the propagation of uncertainty that accounted for lack of knowledge about the dates of change of residence and/or change in milk sources did not function as originally intended. For 783 subjects, the uncertainty in the date of change of a residence or the date of change of a milk source exceeded 1 month. Among those 783 subjects, 173 had uncertainty of more than 1 month in the date of change of residence, and 610 subjects had uncertainty of more than 1 month in the date of change of a milk source. Therefore, for the purposes of Phase IIR, each of the individuals who had uncertainty greater than 1 month in their dates of change of residence or diet, 10 random months were selected within the interval of time specified by the subject to be uncertain. For each month

[4] Correlations used previously were 1.0 between external exposure and inhalation, external exposure and internal dose from consumption of milk from a backyard cow, and external exposure and internal dose from locally grown vegetables; otherwise, correlations were taken to be 0.0.

[5] For Phase II a maximum correlation of 0.8 was assumed for events occurring within the same month. A reduction in correlation was applied according to −0.01 per month lapse between events.

selected, the exact date of change in either residence or diet was assumed as the 15th day of the selected month.

For the Phase IIR doses reported here, we calculated 10 alternative realizations of the total dose and its uncertainty from the 10 random months selected. Those 10 alternative realizations of total dose and uncertainty were then used to calculate the total mean dose for the subject. The uncertainty in the total mean dose is calculated by adding the arithmetic variance from the 10 realizations of mean dose to the arithmetic variance obtained from averaging the 10 unique realizations of dose uncertainty across the 10 realizations. This is shown in Eq. (7),

$$U^2_{(\text{total dose})} = U^2_{(10\ \text{realizations})} + U^2_{(\text{average dose})}, \quad (7)$$

where U^2 is the arithmetic variance. It is recognized that this approach is only an approximation of the total uncertainty associated with the lack of knowledge about the date of change of residence and/or the date of change in milk source. This approximation is preferred, however, to the assumption of a single default date that might be used as a surrogate to the true date of change, as has been performed in other dose reconstructions [see, for example, Kopecky *et al.* (*46*)]. Further analysis of this important source of uncertainty will be considered in Phase III of the Utah TCS, for which we will employ a full Monte Carlo error-propagation method as a replacement for the algebraic error-propagation equations employed in Phases II and IIR.

Quality Assurance/Quality Control Program

Due to the improper and, in some cases, incomplete operation of the Phase II dosimetry programs, the doses reported earlier for Phase II (*9*) are now recognized to have had inaccuracies that required correction. In the Phase IIR study discussed here, extensive steps have been taken to ensure the proper operation of the software used to estimate individual doses. That is, many steps were taken to ensure that the doses were recalculated according to the originally published algorithm (*8*), except for minor corrections as described above.

The first quality assurance (QA) step that evolved was very important, although it was not initially planned as a QA measure. This was the calculation of the entire set of cohort doses by two different programmers working independently on two different computer hardware platforms in two different programming languages. This use of two parallel computing paths originated because of doubts about whether either system could be used successfully to perform all the calculations. The two systems used to perform the Phase IIR calculations (Analytica®[6] and BASE SAS® Vs. 9[7]) differ substantially in their design and means of implementation. Analytica® is a visual programming tool for creating, analyzing and communicating decision models, uses object-type ''influence diagrams'', and includes a built-in Monte Carlo engine for simulations. BASE SAS® Vs. 9 is a widely used programming language and is part of a large commercial statistical analysis system. Eventually, both systems were used successfully to perform the needed dosimetry calculations, though several months were required to debug the calculations in both systems.

All databases were examined in detail to ensure their correctness prior to production of final dose estimates. The processes we implemented to ensure the quality of the databases included range checks and verification of random samples of data. For range checks, this typically consisted of reviewing the higher 1% and lower 1% of data values to ensure that the values at the extremes were correct and reasonable. In addition, 1% of the values were chosen at random with the use of a random-number generator and then checked. In all cases, the values were checked against the most original set of data.

Once the databases were corrected and/or verified as correct, check sums were calculated and the databases were ''locked'' so that unauthorized persons could not modify them. As an added precaution against catastrophic loss, copies of all electronic data sets were stored at two offsite locations.

[6] Lumina Decision Systems, Inc., Los Gatos, CA.
[7] SAS Institute, Inc., Cary, NC.

Another QA step pertained to the estimation of doses outside of Utah and the surrounding states. For Phase IIR, unlike for Phase II, we used the NCI dose calculator (*42*) to estimate doses when subjects lived outside the immediate areas covered by the TDB, the CDB or the OLDB. Repetitive calculations of those doses involving multiple entries of residence and consumption-rate histories were carried out. In cases where discrepancies were found among calculated values, a different person re-entered the data for a third calculation to determine the correct estimate.

After the final doses were calculated, an additional series of QA checks were made. These steps included reviewing the higher and lower doses for reasonableness. For example, we examined whether a person's exposure history would have logically produced the extremes of dose. In addition, persons with higher and lower values of calculated uncertainty were reviewed to determine whether such extreme values were logical. To assist in the review process, 10 persons were identified as ''sentinel'' individuals, and their calculated doses were noted carefully from time to time to ensure that their estimated doses had not changed for inexplicable reasons.

As a final check, doses for a few individuals were calculated independently with the use of a conventional computer spreadsheet. This turned out to be a very difficult task for subjects who had moved frequently or had changed sources of milk frequently, especially if the sources from which milk was purchased involved complicated pools of local producers. Further work on this independent calculation process would have been desirable in the absence of the verification of the doses by the use of the two independent platforms. It is our judgment that the use of the two independent programmers and software systems was the most significant QA mechanism we implemented; however, the verification of all databases used in the calculations against original sources was also an important activity.

RESULTS

The results of the Phase IIR dose calculations differ in several ways from the reported Phase II calculations (*9*). In particular, the revised calculations have resulted in changes to individual mean doses and mean values of subpopulations (Table 2), as well as changes to the cumulative distribution of individual geometric mean dose estimates (Fig. 2, left panel) and calculated geometric standard deviations of individual doses (Fig. 2, right panel). The changes in Phase IIR, while numerous, could be mistaken to be inconsequential unless viewed in detail (Figs. 2, 3 and 4), as shown and discussed here.

General Comparison of the Phase II and Phase IIR Results

We examined changes in estimated doses from Phase II to Phase IIR as a complete data set and in subsets defined by the residences of study subjects on the date of detonation of test HARRY (May 19, 1953). We segregated individuals for comparison purposes into groups defined by their residence on that date: (1) all locations together, (2) residence in Graham County, Arizona (the original location for control subjects for this study), (3) residence in Lincoln County or Washington County, (4) residence in locations other than Lincoln County, Washington County or Graham County, and (5) conceived after May 19, 1953. Summary statistics are presented in Table 2 for each of the five groups.

For the group of all subjects together, the mean dose increased by only about 10%, from 0.11 to 0.12 Gy. The

TABLE 2
Summary Statistics Comparing Point Estimates of Thyroid Dose (Arithmetic Mean) for Individuals in Phase II and Phase IIR

Group and summary statistics	Phase II	Phase IIR	Ratio (IIR/II) (unitless)
All locations together			
Number of subjects	2473	2497	1.01
Minimum (Gy)	0	0.00011	—
Maximum (Gy)	4.6	1.4	0.31
Median (Gy)	0.035	0.055	1.6
Mean (Gy)	0.11	0.12	1.1
Variance (Gy^2)	0.036	0.028	0.78
Residence in Graham County on May 19, 1953[a]			
Number of subjects	382	382	1.00
Minimum (Gy)	0.012	0.00023	0.018
Maximum (Gy)	0.38	0.46	1.2
Median (Gy)	0.0046	0.0016	0.34
Mean (Gy)	0.013	0.016	1.2
Variance (Gy^2)	0.0015	0.0013	0.90
Residence in Lincoln County or Washington County on May 19, 1953[a]			
Number of subjects	960	968	1.01
Minimum (Gy)	0.013	0.00018	0.013
Maximum (Gy)	4.6	1.4	0.31
Median (Gy)	0.16	0.14	0.88
Mean (Gy)	0.22	0.22	0.99
Variance (Gy^2)	0.064	0.047	0.74
Residence at locations other than in Lincoln County, Washington County, or Graham County on May 19, 1953[a]			
Number of subjects	594	607	1.02
Minimum (Gy)	0	0.00019	—
Maximum (Gy)	0.89	0.72	0.81
Median (Gy)	0.012	0.055	4.8
Mean (Gy)	0.042	0.080	1.9
Variance (Gy^2)	0.0082	0.0081	0.99
Conceived[b] after May 19, 1953			
Number of subjects	537	540	1.01
Minimum (Gy)	0	0.00011	—
Maximum (Gy)	0.39	0.30	0.78
Median (Gy)	0.013	0.022	1.7
Mean (Gy)	0.027	0.039	1.4
Variance (Gy^2)	0.0017	0.0021	1.2

[a] May 19, 1953 was the detonation date of shot HARRY.
[b] Conception date of May 19, 1953, was assumed as equivalent to birth date of Feb. 17, 1954.

cumulative distributions of individual geometric mean doses were similar (Fig. 2, left panel) except for the lower 10% that increased substantially, primarily due to use of the NCI dose calculator. Examination of subsets of the dose data by location of residence on May 19, 1953 (Table 2) indicates that estimates of dose in Lincoln County, Washington County and Graham County, Arizona, did not change greatly *on average*, but there was about a twofold increase in the mean of individual doses for those living outside of those areas. Here again, the input of doses from the NCI dose calculator had significant influence on the Phase IIR results.

Even though the mean of individual doses within the groups defined by residence on May 19, 1954, did not change greatly, there were portions of each group that did change substantially. The degree of change in doses from Phase II to Phase IIR is illustrated in Fig. 3 by histograms of the ratio of dose (Phase IIR/Phase II). The Lincoln County, NV, and Washington County, UT, group had the least amount of change; nearly 70% of the Phase IIR estimates remained between two times smaller and two times larger than in Phase II. The Arizona group had the largest proportion changing to smaller values; over one-third of that group decreased in Phase IIR to between one-half and one-tenth of the Phase II values. Conversely, the group conceived after May 19, 1953, had the largest proportion of changes to higher values; nearly 20% increased by more than 10 times.

The correlation between Phase II and Phase IIR doses is shown in Fig. 4, where the arithmetic mean doses for each subject are indicated according to location of residence in May 1953. The strongest relationship between the old and new values was for Lincoln County and Washington County. The weakest relationship was for locations other than Lincoln and Washington Counties and Arizona. Those other locations would include, of course, locations outside of Utah and surrounding states where the NCI dose calculator was used to assign non-zero doses to persons previously assigned zero doses.

Changes Related to Modifications of the Soil Ingestion Model for Grazing Animals

Modifications to the model for ingestion of soil by grazing animals, as noted earlier, resulted in a decrease of the estimates of intake of radioiodines. Similarly, the maximum estimated doses decreased significantly in Phase IIR (see Table 2) due to those modifications. For example, the Phase IIR estimates of the maximum doses for persons residing in Lincoln County and Washington County on May 19, 1953, are only about one-third the values estimated during Phase II. The most dramatic effect can be explained by the following reason. The model of interception of fallout by vegetation (*8, 41*) incorporated into both the Phase II and Phase IIR models results in a larger proportion of fallout that falls directly onto the soil (i.e., is not intercepted by plants) at close-in locations, compared to more distant locations, because of the predominance of moderately large particles at close-in distances. Increasing the effective depth from which animals ingest soil, as was done for the Phase IIR calculations, reduces the area of contaminated soil from which animals are assumed to consume soil. These changes effectively reduce the estimated intake of radioiodine by dairy animals and lead to reduction in dose from consuming animal milk.

Changes Related to Use of the NCI Dose Calculator

The lower doses (i.e., the lower 10–15%) in Phase II were often for individuals living outside of Utah and the

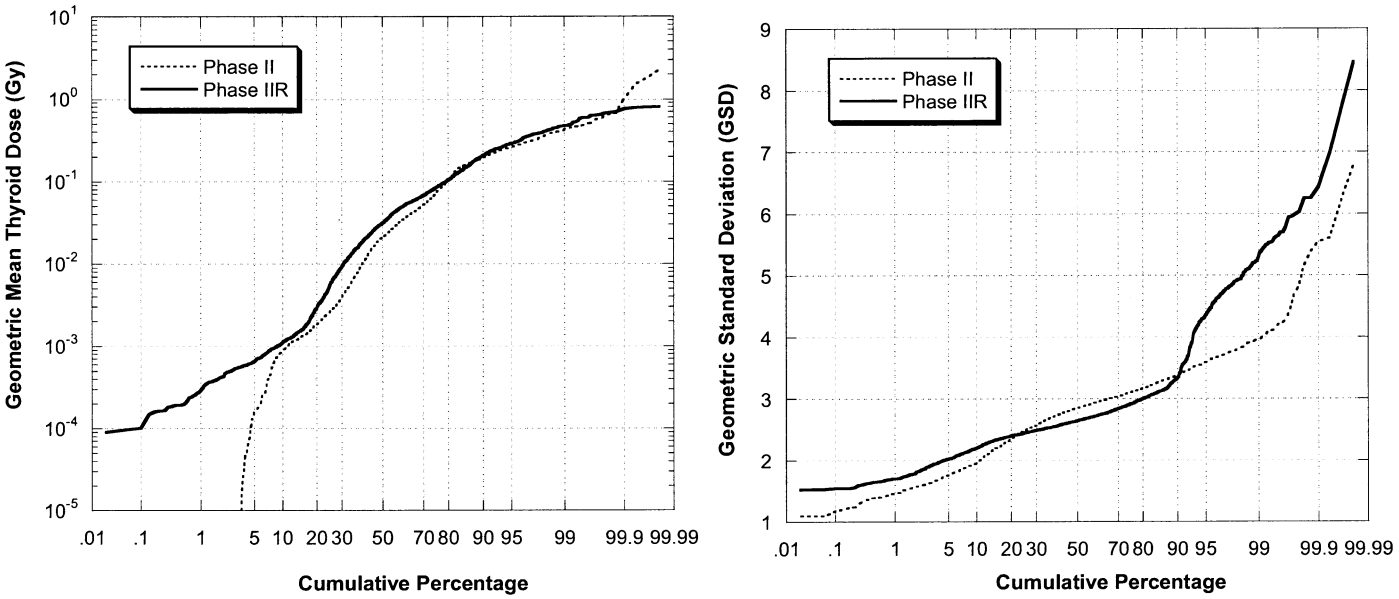

FIG. 2. Comparison of cumulative probability distributions of geometric mean (GM) thyroid dose estimates (mGy) from Phase II (n = 2473) and Phase IIR (n = 2497) (left panel), and geometric standard deviations (GSDs) of thyroid absorbed dose estimates in Phase II and Phase IIR (right panel). Note that the lowest 3% (66 individuals) of the Phase II distribution has assigned doses of 0.0 and are included, although they are off-scale.

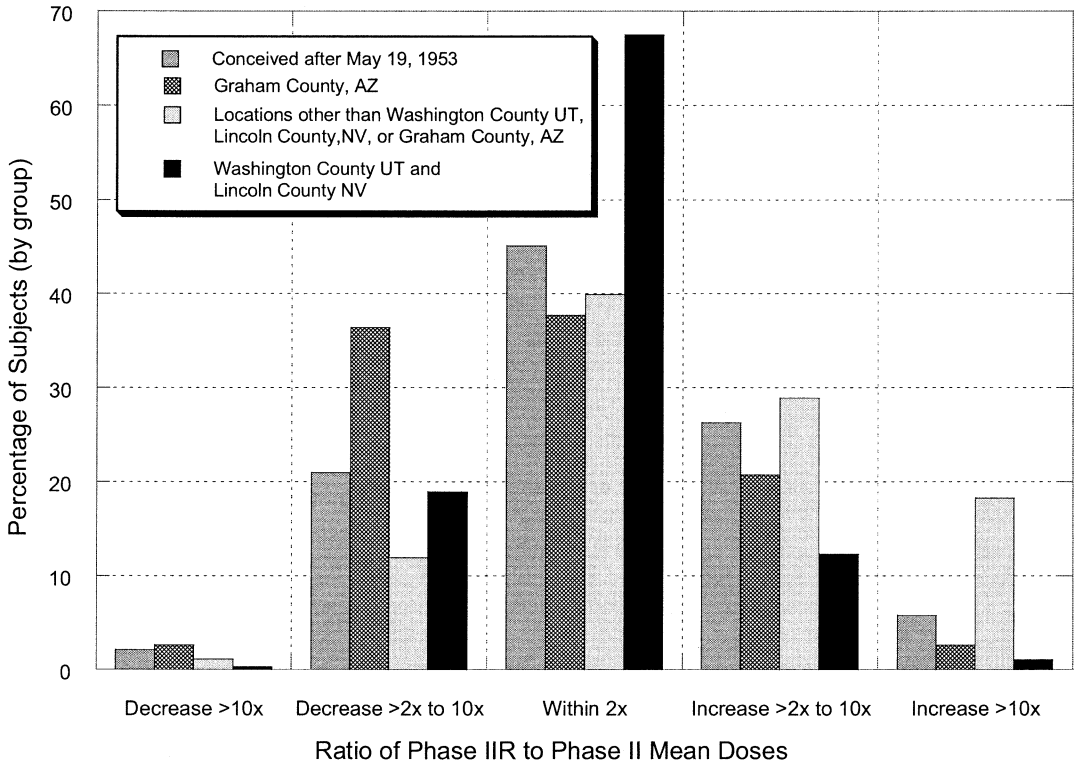

FIG. 3. Distributions of ratios of Phase IIR to Phase II arithmetic mean dose estimates for individuals, grouped by residence location on May 19, 1953: Graham County, AZ (checkered), Lincoln County, NV and Washington County, UT (black), locations other than Lincoln County, NV, Washington County, UT or Graham County, AZ (light gray), conceived after May 19, 1953 (dark gray). See Table 2 for number of subjects in each group. Subjects assigned zero dose in Phase II are not included.

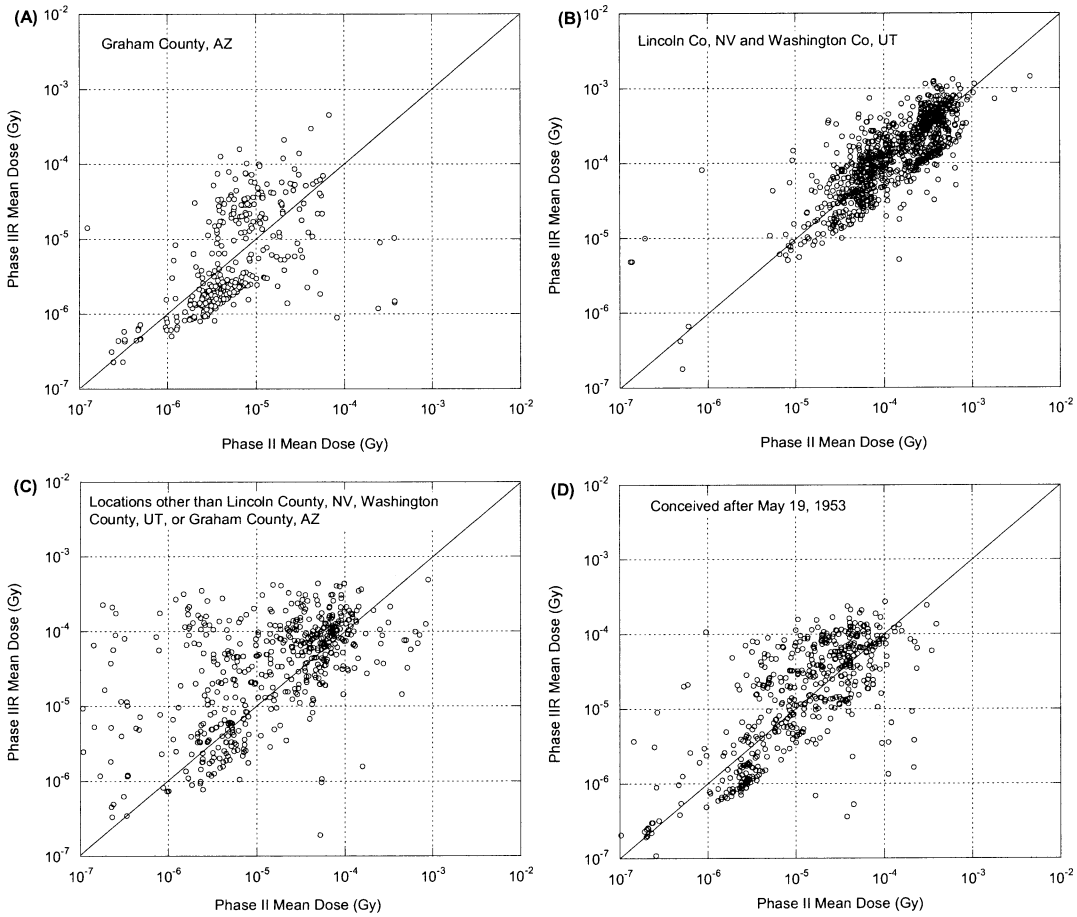

FIG. 4. Phase II arithmetic mean thyroid absorbed dose (mGy) estimates (abscissa) as a function of Phase IIR values (mGy, ordinate) by residence location on May 19, 1953.

surrounding states at the time of the more significant deposition events. For individuals residing outside the seven-state area at the time of testing, doses for Phase IIR were estimated using the NCI dose calculator (*42*). The lower 10% of the earlier calculated doses increased substantially (see Fig. 2, left panel) as a result.

There were 299 persons for whom some or all of their thyroid dose was estimated using the NCI calculator. Of those, 50% received NCI-derived estimates that comprised 90% or more of their total dose estimate; the total mean doses for these subjects ranged from less than 0.001 Gy to 0.72 Gy.

For 66 of the 299 persons for whom some or all of their thyroid dose was estimated using the NCI dose calculator, a zero dose had previously been assigned in Phase II. In Phase IIR, the average of the mean total thyroid dose estimated for those same persons using the NCI calculator was 0.12 Gy, with a range from 0.007 to 0.72 Gy.

Changes Related to Modification of the Transfer Coefficient for Mother's Milk

As discussed earlier, in the Phase IIR dosimetry, the coefficient describing the transfer of ^{131}I and ^{133}I to mother's breast milk was increased substantially over the value assumed in the Phase II dosimetry. There were 212 persons nursing at the time of arrival of fallout from at least one shot. For 27% of these persons, the dose from consumption of mother's milk comprised at least 30% of their total thyroid dose. For three persons, their individual mean dose from consumption of mother's milk was at least 90% of the total thyroid dose. For 75 persons, the range of the Phase IIR individual mean thyroid dose from consumption of mother's milk was from 0.01 Gy to 0.59 Gy.

Uncertainties in Dose

In both Phases II and IIR, the uncertainty of individual doses was expressed as a geometric standard deviation (GSD). Figure 2 (right panel) demonstrates that the uncertainty on total estimated doses varied considerably throughout the cohort in both phases. Between the 10th and 90th percentiles of the cumulative distribution of the GSDs for individual estimates, the range and the shape of the cumulative distribution did not change greatly from Phase II calculations; the 50th percentile of the GSD for Phase IIR at about 2.5 was slightly less than the median of 2.9 for Phase II. However, below the 10th percentile and above the

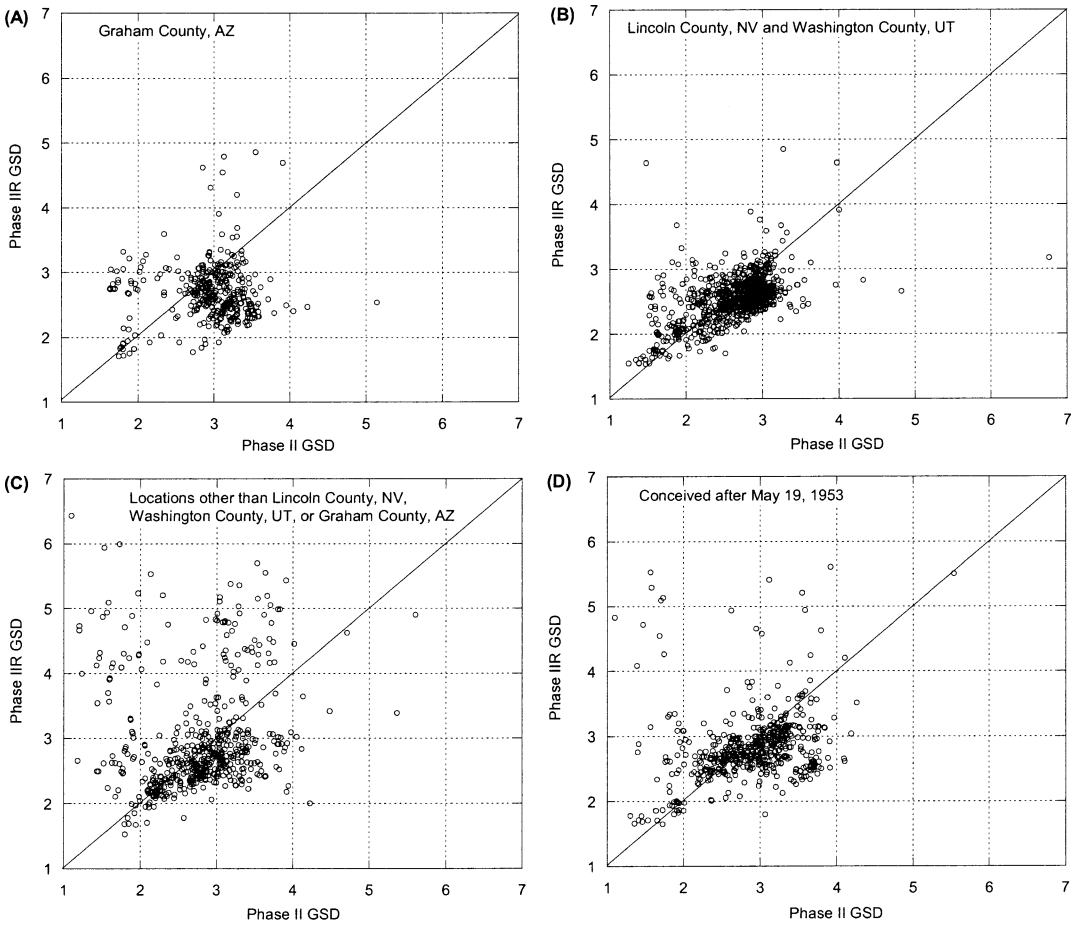

FIG. 5. Phase II GSD (abscissa) of individual doses as a function of Phase IIR GSD (ordinate) by residence location on May 19, 1953.

90th percentile, the GSD of the individual dose estimates for Phase IIR were markedly larger than estimated in Phase II. The distribution of individual GSDs for Phase IIR ranged from about 1.5 to 8.5 (see Fig. 2, right panel).

Figure 5 presents scatter plots of the GSD values in Phase II and Phase IIR, with indication by location of residence in May 1953. Similar to the case for mean dose (Fig. 4), the relationship of the Phase II and Phase IIR GSDs was strongest for Lincoln County and Washington County and weakest for other locations.

Not obvious from Figs. 2, 3, 4 or 5 are the concurrent changes in the geometric mean (GM) dose and the related GSD for individuals. The relationships of GM and GSD for Phase II and IIR are compared in Fig. 6 in the form of scatter plots. Though no simple interpretation of the patterns can be made, it is clear that in the revised dose set (Phase IIR), there were few doses below 0.1 mGy and no GSDs below 1.5, and new estimates of dose did not necessarily maintain the same uncertainty (GSD) as was estimated in Phase II.

DISCUSSION

In Phase IIR, a complex series of data files have been developed containing information from interviews of study subject's parents or nearest relatives describing individual residence histories, dietary habits, and milk sources for 2497 persons and the description of agricultural practices of 1597 different producers of milk. These data files have been combined with additional data files describing localized differences in fallout from 75 nuclear tests. The combined data are used as input to two independent computer codes that implement mathematical algorithms to estimate quantitatively the deposition of ^{131}I and ^{133}I onto vegetation and soil, its transfer to milk, and the resulting thyroid dose for individuals and the related uncertainty in dose. The computations include models for external exposure from fallout deposited on the ground surface as well as inhalation of radioactive fallout.

The complexities inherent in the combination of complex data files and computerized mathematical exposure pathway and dose algorithms present considerable opportunities for errors in data management and computations, some of these errors escaped detection in previous work (*9, 10, 14*).

To improve the reliability of the dose estimates obtained in Phase IIR, substantial improvements have been made to the overall dose reconstruction procedure to ensure a rigorous QA/QC of the calculated results. Phase IIR is perhaps

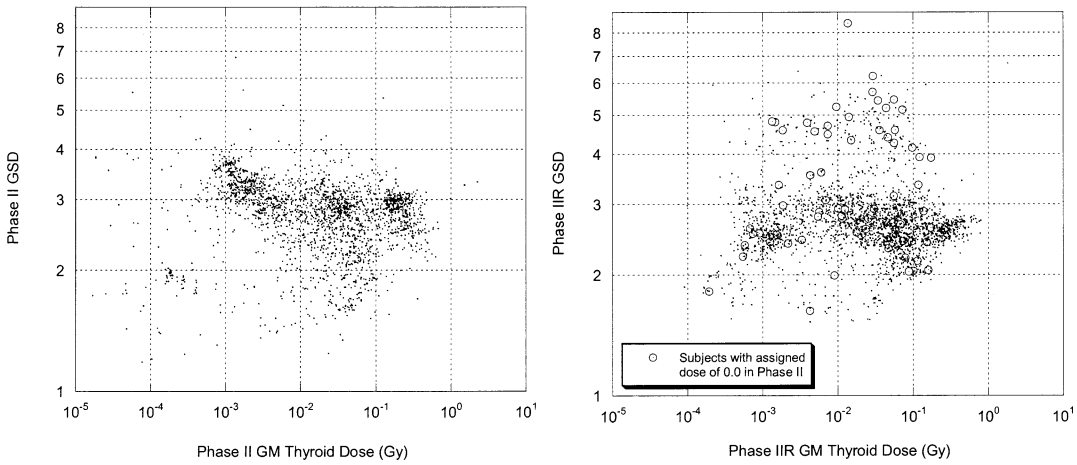

FIG. 6. Relationships between individual geometric mean (GM) dose estimates and geometric standard deviations (GSD) in Phase II (left panel) and in Phase IIR calculations (right panel). Open circles in right panel are those subjects ($n = 66$) assigned a dose of 0.0 in Phase II.

the first dose reconstruction of its kind to incorporate such a high level of quality assurance.

The comparison of summary statistics between Phase II and Phase IIR (Table 2) shows that most statistical results changed by less than 30%; a few statistics, however, indicated that significant changes occurred. For example, the maximum of individual mean doses for the entire cohort and the median of individual mean doses for those who resided in Graham County, Arizona, on May 19, 1953, decreased by about a factor of three, while the median of individual doses for those residing outside of Graham, Lincoln and Washington Counties increased by almost a factor of five.

Substantially larger differences are revealed when comparing scatter plots of doses for individual members of the cohort (Figs. 3, 4 and 5). For those who resided in Lincoln County and Washington County, the doses changed by a factor of about 2 to 3 for the following reasons. Doses increased in Phase IIR due as a result of correction of coding errors related to the contribution to the animals' diet from fallout deposition on fresh pasture, and doses decreased due to changes in assumptions about the average depth of soil consumed by cows and goats.

The effect of correcting coding errors for the animals' consumption of contaminated fresh pasture was more pronounced for locations more distant from the Nevada Test Site than for Lincoln and Washington Counties, because at more distant locations fallout occurred as fine particles and was readily retained on the surfaces of vegetation. Thus the ingestion of contaminated soil would have been much less important at locations where there was high interception of fallout on vegetation surfaces.

The largest differences between Phase II and Phase IIR doses are evident for those who resided in regions outside of Graham, Lincoln and Washington Counties before May 19, 1953. In general, Phase II doses less than 0.01 Gy were increased by one or more orders of magnitude in Phase IIR. This primarily reflects the use of the NCI dose calculator (*42*) to estimate doses for individuals exposed to fallout when they resided outside the seven-state study area (Fig. 1, right panel). In Phase II, 299 persons received at least a partial dose of zero for the times when exposures occurred outside of the seven-state study area; for 66 persons, a total thyroid dose of zero had been assigned. In Phase IIR, no individual were assigned a zero dose.

In evaluating the differences in uncertainty estimates for individual doses (Fig. 5), there appears to be only a moderate degree of correlation between the results of Phase II and Phase IIR. Means of the estimated GSDs in Phase IIR are similar to those in Phase II, though the upper 10% of the 2497 values estimated in Phase IIR are substantially greater than those calculated in Phase II. About 90% of all estimated GSDs fall between 2 and 4.

The reasons for the variation in the dose uncertainties are numerous and complex; however, the lower uncertainties appear to be representative of individuals exposed primarily by inhalation and to external radiation from ground depositions resulting from multiple fallout events. For those who resided primarily in one to a few locations and who consumed milk from pooled milk sources such as a grocery store or large commercial dairies, the GSD ranged from slightly above 2.0 to about 3.0. Larger uncertainties were estimated for those whose milk was obtained from a family cow or goat. For these persons, the GSDs of the estimated dose were generally of the order of 2.6 to more than 3.0.

Individual thyroid dose GSDs of the order of 4.0 or more were usually representative of persons consuming fresh milk and who had a complex and uncertain residence history. The larger dose uncertainties, those with GSDs exceeding 6.0, were often the result of exposure to a few fallout events whose depositions were based on estimates made using atmospheric transport models in the absence of fallout measurements on soil or gummed film at locations beyond the seven states of the original study. Such esti-

mates were usually associated with tests conducted very early or late in the testing program when monitoring was minimal. For those situations, dose estimates were made using the NCI dose calculator.

The GSDs for those who resided in Lincoln and Washington Counties on May 19, 1953, appear to have not changed as much as for those who lived elsewhere; this appears to have been influenced in part by the fact that there were relatively fewer residence moves for those who lived in those counties (an average of 2.5 residence changes) and in Graham County (an average of 1.7 residence changes) compared with those who lived outside of these areas (an average of 3.8 changes in residence history).

It is of some importance to understand that two separate methodologies were used to calculate doses for this Phase IIR study. As we have described, an updated application of the Phase II method was used for residents in the seven-state area only, while the NCI dose calculator (*42*) was used for those living beyond the seven-state area for some period of time but within the 48 contiguous states. Here we call attention to the fact that the Phase II (and Phase IIR) method was developed with the assumption that only dry deposition occurred, since significant care was taken by the responsible authorities not to test nuclear devices when rain was expected in the near downwind area. On the other hand, the NCI method (*11*) was applied to locations further downwind, particularly in the eastern U.S., where wet deposition was likely a substantial consideration. Continued follow-up of this cohort will be accompanied by additional improvements in dosimetry that will include, among other things, establishing a national data base of ^{137}Cs deposition values such that the entire country is treated uniformly with respect to retention of fallout by vegetation, regardless of whether wet or dry deposition was involved.

CONCLUDING REMARKS

Since the late 1980s when the Phase II dose reconstruction was completed, additional studies of the dose to humans from fallout have been undertaken, and the methods used have been similar, though generally not as specific for individual dose assessment. Notable examples are the NCI (*11*) study of the dose to the thyroid from NTS ^{131}I at all locations in the contiguous United States. For that study, a national database of daily ^{131}I deposition in every county was prepared using methods similar to those used for the preparation of the Town and County Data Bases. Another example of a study recently completed with the use of the actual ORERP methods is the joint feasibility study by the CDC/NCI (*47*) of the dose at all locations in the continental United States from all radionuclides in fallout from the NTS and from global fallout.

The modifications described here as Phase IIR should not be viewed as just an exercise in dose estimation. The Utah Thyroid Cohort Study has been cited extensively as part of the contributing evidence on the health effects due to exposure to ^{131}I (*48–59*), to radioactive fallout from nuclear testing (*60–71*), and as part of the greater body of literature on radiogenic health effects (*72–81*). In addition, because the Utah study first introduced a complex dosimetry system applied to individuals, much interest has been generated in ways to analyze a dose response in the presence of uncertainty (*46, 82–84*). In addition, the Phase IIR modifications were a necessary step in restoring the dosimetry calculations necessary for the Congressionally mandated Phase III of the Utah TCS that is now under way.

Because of the inherent relationship between dose estimates and their uncertainties with the outcome of dose–response analyses, modifications to dose estimates, such as those described here, are essential to deriving firm epidemiological conclusions. The overall effects on the risk analyses due to the Phase IIR revisions to dose estimates have been evaluated and are being prepared for publication. An important result is the now-identified statistically significant dose response for thyroiditis, which was not apparent in the analyses for Phase II.

The process of identifying the modifications necessary for Phase IIR has also been useful in the broader context of developing means to establish and ensure that valid dose estimates are produced when complex algorithms are employed. The revisions and improvements made to the Phase IIR dosimetry system have revealed numerous, if not formidable, challenges in computer programming, data management and QA/QC. The experience here is likely to be similar to other large dose reconstruction studies, where mathematical models have been relied on to reconstruct doses to thousands of subjects in the absence of direct measurements of individual exposures.

ACKNOWLEDGMENTS

The work reported here was funded by the Centers for Disease Control and Prevention through cooperative agreement no. U50/CCU816245 with the University of Utah. We are indebted to the following individuals for their contributions: Steven C. Alder, Judy Allred, Candice Anderson, Randy Baker, Larry Bonnette, Justin Brown, Darlene Buist, Becky Crockett, Sara Feltz, Julie Fryer, Marianoosh Ghodrat, Don Gren, Nikki Konesavanh and Patrice Secrist.

Received: March 4, 2005; accepted: August 26, 2005

REFERENCES

1. U.S. Congress, *The Nature of Radioactive Fallout and its Effects on Man.* Hearings before the Special Subcommittee on Radiation, Joint Committee on Atomic Energy, 85th Congress, U.S. Government Printing Office, Washington, DC, 1957.
2. U.S. Congress, *Fallout from Nuclear Weapons Tests.* Hearings before the Special Subcommittee on Radiation, Joint Committee on Atomic Energy, 86th Congress, U.S. Government Printing Office, Washington, DC, 1959.
3. U.S. Congress, *Fallout, Radiation Standards, and Countermeasures.* Hearings before the Subcommittee on Research, Development and Radiation, Joint Committee on Atomic Energy, 88th Congress, U.S. Government Printing Office, Washington, DC, 1963.
4. E. S. Weiss, M. L. Rallison, W. T. London and G. D. C. Thompson,

Thyroid nodularity in southwestern Utah children exposed to fallout radiation. *Am. J. Public Health* **61**, 241–249 (1971).

5. E. S. Weiss, R. E. Olsen, G. D. C. Thompson and A. T. Masi, Surgically treated thyroid disease among young people in Utah, 1948–1962. *Am. J. Public Health* **57**, 1807–1814 (1967).
6. J. L. Lyon, M. Klauber, J. W. Gardner and K. S. Udall, Childhood leukemias associated with fallout from nuclear tests. *New Engl. J. Med.* **300**, 397–402 (1979).
7. D. C. Gren, H. A. Hawthorne, R. D. Lloyd, S. L. Simon, J. E. Till, R. A. Crockett and W. Stevens, *Feeding of Dairy Livestock and Milk Distribution for the Thyroid Cohort Study*. University of Utah Department of Family and Preventive Medicine, Salt Lake City, 1988.
8. S. L. Simon, R. D. Lloyd, J. E. Till, H. W. Hawthorne, D. C. Gren, M. L. Rallison and W. Stevens, Development of a method to estimate thyroid dose from fallout radioiodine in a cohort study. *Health Phys.* **59**, 669–691 (1990).
9. J. E. Till, S. L. Simon, R. Kerber, R. D. Lloyd, W. Stevens, D. C. Thomas, J. L. Lyon and S. Preston-Martin, The Utah Thyroid Cohort Study: Analysis of the dosimetry results. *Health Phys.* **68**, 472–483 (1995).
10. R. A. Kerber, J. E. Till, S. L. Simon, J. L. Lyon, D. C. Thomas, S. Preston-Martin, M. L. Rallison, R. D. Lloyd and W. Stevens, A cohort study of thyroid disease in relation to fallout from nuclear weapons testing. *J. Am. Med. Assoc.* **270**, 2076–2082 (1993).
11. U.S. National Cancer Institute, *Estimated Exposures and Thyroid Doses Received by the American People from Iodine-131 in Fallout following Nevada Atmospheric Nuclear Bomb Tests*. U.S. National Cancer Institute, Bethesda, MD, 1997.
12. U.S. Congress, *National Cancer Institute's Management of Radiation Studies*. Hearings before the Permanent Subcommittee on Investigations of the Committee on Governmental Affairs, U.S. Senate, 105th Congress, U.S. Government Printing Office, Washington, DC, 1998.
13. U.S. Congress, *Departments of Labor, Health and Human Services, and Education and Related Agencies Appropriation Bill, 1999*. Senate Appropriations Bill Report 105-300, U.S. Senate, 105th Congress, U.S. Government Printing Office, Washington, DC, 1998.
14. W. Stevens, J. E. Till, D. C. Thomas, J. L. Lyon, R. A. Kerber, S. Preston-Martin, S. L. Simon, M. L. Rallison and R. D. Lloyd, *Report of a Cohort Study of Thyroid Disease and Radioactive Fallout from the Nevada Test Site*. University of Utah Department of Family and Preventive Medicine, Salt Lake City, 1992.
15. H. A. Knapp, *Iodine-131 in Fresh Milk and Human Thyroids Following a Single Deposition of Nuclear Test Fallout*. TID-19266, U.S. Atomic Energy Commission, Division of Biology and Medicine, Fallout Studies Branch, Washington, DC, 1963.
16. B. W. Church, D. L. Wheeler, C. M. Campbell, R. V. Nutley and L. R. Anspaugh, Overview of the Department of Energy's Off-Site Radiation Exposure Review Project (ORERP). *Health Phys.* **59**, 503–510 (1990).
17. H. L. Beck, *Exposure Rate Conversion Factors for Radionuclides Deposited on the Ground*. EML-378, U.S. Department of Energy, Environmental Measurements Laboratory, New York, 1980.
18. H. G. Hicks, Calculation of the concentration of any radionuclide deposited on the ground by off-site fallout from a nuclear detonation. *Health Phys.* **42**, 585–600 (1982).
19. H. L. Beck, *Estimates of Fallout from Nevada Weapons Testing in the Western United States Based on Gummed Film Monitoring Data*. EML-433, U.S. Department of Energy, Environmental Measurements Laboratory, New York, 1984.
20. F. W. Whicker and T. Kirchner, PATHWAY: A dynamic food chain model to predict radionuclide ingestion after fallout deposition. *Health Phys.* **52**, 717–737 (1987).
21. D. D. Breshears, T. B. Kirchner, M. O. Otis and F. W. Whicker, Uncertainty in predictions of fallout radionuclides in foods and of subsequent ingestion. *Health Phys.* **57**, 943–953 (1989).
22. R. W. Henderson and R. F. Smale, External exposure estimates for individuals near the Nevada Test Site. *Health Phys.* **59**, 715–721 (1990).
23. H. G. Hicks, Additional calculations of radionuclide production following nuclear explosions and Pu isotopic ratios for Nevada Test Site events. *Health Phys.* **59**, 515–523 (1990).
24. Y. C. Ng, L. R. Anspaugh and R. T. Cederwall, ORERP internal dose estimates for individuals. *Health Phys.* **59**, 693–713 (1990).
25. V. E. Quinn, Analysis of meteorological and radiological data for selected fallout episodes. *Health Phys.* **59**, 577–592 (1990).
26. G. M. Ward and F. W. Whicker, Milk distribution and feeding practice data for the PATHWAY model. *Health Phys.* **59**, 637–43 (1990).
27. F. W. Whicker, T. B. Kirchner, D. D. Breshears and M. D. Otis, Estimation of radionuclide ingestion: The ''PATHWAY'' food-chain model. *Health Phys.* **59**, 645–657 (1990).
28. C. B. Thompson, Estimates of exposure rates and fallout arrival times near the Nevada Test Site. *Health Phys.* **59**, 555–563 (1990).
29. H. L. Beck and L. R. Anspaugh, *Development of the County Data Base: Estimates of Exposure Rates and Times of Arrival of Fallout in the ORERP Phase-II Area. Comparison with Cumulative Deposition Estimates Based on Analyses of Retrospective and Historical Soil Samples*. Report NVO-320, U.S. Department of Energy, Nevada Operations Office, Las Vegas, 1991.
30. C. B. Thompson, R. D. McArthur and S. W. Hutchinson, *Development of the Town Data Base: Estimates of Exposure Rates and Times of Fallout Arrival near the Nevada Test Site*. Report DOE/NV-374, U.S. Department of Energy, Nevada Operations Office, Las Vegas, 1994.
31. L. R. Anspaugh and B. W. Church, Historical estimates of external γ exposure and collective external γ exposure from testing at the Nevada Test Site. I. Test series through Hardtack II, 1958. *Health Phys.* **51**, 35–51 (1986).
32. L. R. Anspaugh, Y. E. Ricker, S. C. Black, R. F. Grossman, D. L. Wheeler, B. W. Church and V. E. Quinn, Historical estimates of external γ exposure and collective external γ exposure from testing at the Nevada Test Site. II. Test series after Hardtack II, 1958, and summary. *Health Phys.* **59**, 525–532 (1990).
33. NCRP, *SI Units in Radiation Protection and Measurements*. Report No. 82, National Council on Radiation Protection and Measurements, Bethesda, MD, 1985.
34. G. D. Potter, Film badge and survey-meter databases for historical off-site radiation exposures around the Nevada Test Site. *Health Phys.* **50**, 424 (1986).
35. R. F. Grossman and C. B. Thompson, *Creation of a Database of Survey Meter Readings in the Western United States after Nuclear Tests*. Report EPA/600/R-93/034, U.S. Environmental Protection Agency, Las Vegas, 1993.
36. H. G. Hicks, *Radiochemical Data Collected on Events from which Radioactivity Escaped Beyond the Borders of the Nevada Test Range Complex*. Report UCRL-52934, University of California, Lawrence Livermore Laboratory, Livermore, 1981.
37. H. G. Hicks, *Results of Calculations of External Gamma Radiation Exposure Rates from Fallout and the Related Radionuclide Compositions, Parts 1–8*. Report UCRL-53152, University of California, Lawrence Livermore Laboratory, Livermore, 1981.
38. Radiation Shielding Information Center, *RSIC Computer Code Collection. ORIGEN-79 Isotope Generation and Depletion Code—Matrix Exponential Method*. Report CCC-217, Oak Ridge National Laboratory, Oak Ridge, 1979.
39. P. W. Krey and H. L. Beck, *The Distribution throughout Utah of ^{137}Cs and $^{239+240}Pu$ from Nevada Test Site Detonations*. Report EML-400, U.S. Environmental Measurements Laboratory, New York, 1981.
40. R. T. Cederwall and K. R. Peterson, Meteorological modeling of arrival and deposition of fallout at intermediate distances downwind of the Nevada Test Site. *Health Phys.* **59**, 593–601 (1990).
41. S. L. Simon, An analysis of vegetation interception data pertaining to close-in weapons test fallout. *Health Phys.* **59**, 619–626 (1990).
42. U.S. National Cancer Institute, *Individual Dose Calculator*. U.S. National Cancer Institute, Bethesda, http://ntsi131.nci.nih.gov/, last accessed on February 6, 2005.

43. E. M. Rupp, Age dependent values of dietary intake for assessing human exposure to environmental pollutants. *Health Phys.* **39**, 151–163 (1980).

44. Y. C. Ng, C. S. Colsher, D. J. Quinn and S. E. Thompson, *Transfer Coefficients for the Prediction of the Dose to Man Via the Forage-Cow-Milk Pathway from Radionuclides Released to the Biosphere.* Report UCRL-51939, University of California, Lawrence Livermore Laboratory, Livermore, 1977.

45. S. L. Simon, N. Luckyanov, A. Bouville, L. VanMiddlesworth and R. M. Weinstock, Transfer of ^{131}I into human breast milk and transfer coefficients for radiological dose assessments. *Health Phys.* **82**, 796–806 (2002).

46. K. J. Kopecky, S. Davis, T. E. Hamilton, M. S. Saporito and L. E. Onstad, Estimation of thyroid radiation doses for the Hanford Thyroid disease study: Results and implications for statistical power of the epidemiological analyses. *Health Phys.* **87**, 15–32 (2004).

47. U.S. Centers for Disease Control and Prevention and U.S. National Cancer Institute, *A Feasibility Study of the Health Consequences to the American Population from Nuclear Weapons Tests Conducted by the United States and other Nations.* U.S. Centers for Disease Control and Prevention, Atlanta, in press.

48. D. J. Brenner, The relative effectiveness of exposure to I-131 at low doses. *Health Phys.* **76**, 180–185 (1999).

49. S. Davis, V. Stepanenko, N. Rivkind, K. J. Kopecky, P. Voilleque, V. Shakhtarin, E. Parshkov, S. Kulikov, E. Lushnikov and A. Tsyb, Risk of thyroid cancer in the Bryansk Oblast of the Russian Federation after the Chernobyl Power Station accident. *Radiat. Res.* **162**, 241–248 (2004).

50. S. Davis, K. J. Kopecky, T. E. Hamilton and L. Onstad, Thyroid neoplasia, autoimmune thyroiditis, and hypothyroidism in persons exposed to iodine 131 from the Hanford Nuclear Site. *J. Am. Med. Assoc.* **292**, 2600–2613 (2004).

51. J. A. Franklyn, P. Maisonneuve, M. Sheppard, J. Betteridge and P. Boyle, Cancer incidence and mortality after radioiodine treatment for hyperthyroidism: A population-based cohort study. *Lancet* **353**, 2111–2115 (1999).

52. K. Hahn, P. Schnell-Inderst, B. Grosche and L. E. Holm, Thyroid cancer after diagnostic administration of iodine-131 in childhood. *Radiat. Res.* **156**, 61–70 (2001).

53. P. Hall, C. J. Furst, A. Mattsson, L. E. Holm, J. D. Boice, Jr. and P. D. Inskip, Thyroid nodularity after diagnostic administration of iodine-131. *Radiat. Res.* **146**, 673–682 (1996).

54. P. Hall, A. Mattsson and J. D. Boice, Thyroid cancer after diagnostic administration of iodine-131. *Radiat. Res.* **145**, 86–92 (1996).

55. P. Jacob, Y. Kenigsberg, I. Zvonova, G. Goulko, E. Buglova, W. F. Heidenreich, A. Golovneva, A. A. Bratilova, V. Drozdovitch and H. G. Paretzke, Childhood exposure due to the Chernobyl accident and thyroid cancer risk in contaminated areas of Belarus and Russia. *Br. J. Cancer* **80**, 1461–1469 (1999).

56. J. Robbins, Lessons from Chernobyl: The event, the aftermath fallout: Radioactive, political, social. *Thyroid* **7**, 189–192 (1997).

57. M. Schlumberger and F. DeVathaire, 131 iodine: Medical use. Carcinogenetic and genetic effects. *Ann. Endocrinol. Paris* **57**, 166–176 (1996).

58. V. A. Stezhko, E. E. Buglova, L. I. Danilova, V. M. Drozd, N. A. Krysenko, N. R. Lesnikova, V. F. Minenko, V. A. Ostapenko, S. V. Petrenko and L. B. Zablotska, A cohort study of thyroid cancer and other thyroid diseases after the Chornobyl accident: Objectives, design and methods. *Radiat. Res.* **161**, 481–492 (2004).

59. C. M. Grossman, R. H. Nussbaum and F. D. Nussbaum, Cancers among residents downwind of the Hanford, Washington, plutonium production site. *Arch. Environ. Health* **58**, 267–274 (2003).

60. W. M. Bice-Stephens, Radiation injuries from military and accidental explosions: A brief historical review. *Mil. Med.* **165**, 275–277 (2000).

61. M. I. Boutte, Compensating for health: The acts and outcomes of atomic testing. *Hum. Organ.* **61**, 41–50 (2002).

62. F. de Vathaire, B. Le Vu and C. Challeton-de Vathaire, Thyroid cancer in French Polynesia between 1985 and 1995: Influence of atmospheric nuclear bomb tests performed at Mururoa and Fangataufa between 1996 and 1974. *Cancer Causes Control* **11**, 59–63 (2000).

63. H. J. Dworkin, Nuclear-weapons testing fallout and thyroid-disease. *J. Am. Med. Assoc.* **271**, 825–826 (1994).

64. E. Frohmberg, R. Goble, V. Sanchez and D. Quigley, The assessment of radiation exposures in native American communities from nuclear weapons testing in Nevada. *Risk Anal.* **20**, 101–111 (2000).

65. E. S. Gilbert, R. Tarone, A. Bouville and E. Ron, Thyroid cancer rates and I-131 doses from Nevada atmospheric nuclear bomb tests. *J. Natl. Cancer Inst.* **90**, 1654–1660 (1998).

66. E. S. Gilbert, C. E. Land and S. L. Simon, Health effects from fallout. *Health Phys.* **82**, 726–735 (2002).

67. R. E. Lapp, Nuclear-weapons testing fallout and thyroid-disease. *J. Am. Med. Assoc.* **271**, 826–826 (1994).

68. J. L. Lyon, Nuclear weapons testing and research efforts to evaluate health effects on exposed populations in the United States. *Epidemiology* **10**, 557–560 (1999).

69. E. Lund and M. R. Galanti, Incidence of thyroid cancer in Scandinavia following fallout from atomic bomb testing: An analysis of birth cohorts. *Cancer Causes Control* **10**, 181–187 (1999).

70. B. S. Richter and H. G. Stockwell, Descriptive study of deaths from cancer associated with residential proximity to the site of underground nuclear detonation. *Arch. Environ. Health* **53**, 109–113 (1998).

71. Z. Zhumadilov, B. I. Gusev, J. Takada, M. Hoshi, A. Kimura, N. Hayakawa and N. Takeichi, Thyroid abnormality trend over time in northeastern regions of Kazakhstan, adjacent to the Semipalatinsk nuclear test site: A case review of pathological findings for 7271 patients. *J. Radiat. Res.* **41**, 35–44 (2000).

72. American Academy of Pediatrics Committee on Environmental Health, Radiation disasters and children. *Pediatrics* **111**, 1455–1466 (2003).

73. J. D. Boice and J. H. Lubin, Occupational and environmental radiation and cancer. *Cancer Causes Control* **8**, 309–322 (1997).

74. R. Doll, Epidemiological evidence of hazard. *Radiat. Prot. Dosim.* **68**, 97–103 (1996).

75. D. L. Fraker, Radiation exposure and other factors that predispose to human thyroid neoplasia. *Surg. Clin. N. Am.* **75**, 365–375 (1995).

76. P. Hall and L. E. Holm, Radiation-associated thyroid cancer—Facts and fiction. *Acta Oncol.* **37**, 325–330 (1998).

77. J. J. Mangano, J. Sherman, C. Chang, A. Dave, E. Feinberg and M. Frimer, Elevated childhood cancer incidence proximate to US nuclear power plants. *Arch. Environ. Health* **58**, 74–82 (2003).

78. C. R. Muirhead, Cancer after nuclear incidents. *Occup. Environ. Med.* **58**, 482–488 (2001).

79. M. F. Prummel, T. Strieder and W. M. Wiersinga, The environment and autoimmune thyroid diseases. *Eur. J. Endocrinol.* **150**, 605–618 (2004).

80. E. Ron, Ionizing radiation and cancer risk: Evidence from epidemiology. *Radiat. Res.* **150** (Suppl.), S30–S41 (1998).

81. R. Wakeford, The cancer epidemiology of radiation. *Oncogene* **23**, 6404–6428 (2004).

82. B. Mallick, F. O. Hoffman and R. J. Carroll, Semiparametric regression modeling with mixtures of Berkson and classical error, with application to fallout from the Nevada test site. *Biometrics* **58**, 13–20 (2002).

83. D. O. Stram and K. Kopecky, Power analysis of epidemiological studies of radiation-related disease risk when dose estimates are based on a complex dosimetry system with an application to the Hanford Thyroid Disease Study. *Radiat. Res.* **158**, 797–798 (2002).

84. D. O. Stram and K. J. Kopecky, Power and uncertainty analysis of epidemiological studies of radiation-related disease risk in which dose estimates are based on a complex dosimetry system: Some observations. *Radiat. Res.* **160**, 408–417 (2003).